Correspondence

Human Growth Hormone—Orphan With a Silver Spoon

To THE EDITOR: Douglas Frasier, a fellow pediatric endocrinologist, indicated that it was inappropriate to consider recombinant human growth hormone as a privileged "orphan" drug under the Orphan Drug Act because that allowed its exclusive producers, Genentech and Eli Lilly, to reap excessive profits.[1] Including this drug in the special orphan category was defended by representatives of Genentech and the Food and Drug Administration (FDA), successfully in my opinion. I agree that the availability of recombinant human growth hormone has proved beneficial and even life-saving in children with growth hormone deficiency. Not only does it prevent dwarfism, but it normalizes facial features and body configuration and prevents the severe hypoglycemia that can lead to brain damage. In view of the limited number of children with hypothalamic or hypopituitary growth deficiency, I think pharmaceutical companies deserve a good return for developing this product.

On the other hand, I am disturbed by efforts to push the use of recombinant growth hormone in children without growth hormone deficiency, including normal, healthy children with short stature and girls with Turner's syndrome. The potential financial bonanza here would make the $200 million profit estimates by Frasier appear to be small change.

We know the effects of excess growth hormone in humans with pituitary gigantism and acromegaly. Not only is height increment accelerated, but coarse thick features appear, there is enlargement of the hands and feet, and diabetes mellitus develops. Growth hormone in vitro increases the growth rate of many cells, raising the specter of neoplasia. Although the recent cases of leukemia in growth-hormone-treated children in Japan were not proved to be due to this treatment,[2] there is still cause for concern, in my mind, particularly in children with Turner's syndrome who have a chromosomal defect.

Genentech has made efforts to ensure the ethical use of its product by distributing it through pediatric endocrinologists. Recombinant human growth hormone is approved by the FDA only for use in growth hormone deficiency. There is now an application for FDA approval for its use in treating Turner's syndrome, however. There is pressure for its use in normal, short children from parents who have been led to think of it as a "height hormone" instead of a substance affecting many cells and metabolic systems.

Lately we have seen evidence here in northern California, the home of Genentech, that marketing people are beginning to prevail over the ethical medical scientists who previously were apparently in control. Pediatricians have been paid honoraria to attend free dinners in San Francisco to hear talks on growth hormone. The largest children's hospital in northern California had a "free growth screening day." Although the above events were sponsored by Genentech, the announcement gave no hint that Genentech was involved. A local Genentech representative mentioned that his income was linked to the amount of growth hormone prescribed in his territory. This same representative was involved in a "height screening program" in public schools in which the parents of short children were advised to see a physician concerning their child's height. A recent private newsletter mailed to all pediatric endocrinologists reported highlights of pediatric research meetings and clearly emphasized the viewpoints of Genentech investigators; the issue was produced by funding from Genentech.[3]

It could be argued that the above activities are simply aggressive marketing aimed at discovering undiagnosed growth hormone deficiency. In my mind, however, these activities are ethically questionable; they represent attempts to expand the use of growth hormone to persons without hormone deficiency and are inappropriate for a privileged orphan drug. In addition, I feel that the manufacturers should be required to show evidence that they are taking measures to prevent recombinant growth hormone from reaching the black market, where the drug is already being abused by athletes and others who can afford the high cost.

The opportunity for growth hormone to become a financial superstar lies in its use in short children without proved growth hormone deficiency (particularly in healthy short children), where its efficacy and long-term safety have not been shown. It is here that we can expect the most pressure to prescribe it, and there is disturbing evidence that few holds will be barred in attempting to reap the immense potential profits. Caveat emptor, FDA.

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REFERENCES

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2. Fisher DA, Job JC, Preece M, et al: Leukaemia in patients treated with growth hormone (Letter). Lancet 1988; 1:1159-1160
3. Clin Courier 1989 Oct; 7:1-11

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Dr Sherman Responds

To THE EDITOR: I welcome the opportunity to respond to Dr Schoen's recent comments about the use of human growth hormone.

Genentech's Protropin (somatrem for injection) is currently indicated for the treatment of short stature associated with growth hormone inadequacy in children. Our commitment to the appropriate use of growth hormone replacement therapy extends to our continuing efforts at monitoring its use in clinical practice. Of the estimated 12,000 patients in the United States currently receiving the therapy, more than half are enrolled and followed in a Genentech-sponsored postmarketing study. The National Cooperative Growth Study was designed, among other things, to disclose unexpected adverse effects of growth hormone treatment. We have now accumulated almost five years of safety- and efficacy-related information in children treated with growth hormone. Treatment-related side effects are rare, and physical changes related to growth hormone excess in children treated with somatrem are essentially unheard of.

In addition, Genentech has in place a very reliable, controlled distribution system for somatrem. This unique distribution system was voluntarily put into place by Genentech, and we think it efficiently mitigates against misuse of the hormone.

Dr Schoen accepts growth hormone for the treatment of children with growth hormone insufficiency but questions its evaluation in other groups of children whose growth is retarded. When only pituitary growth hormone was availa-